

1st ref

10/11/2006 10566558.trn

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PASSWORD:

TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * Welcome to STN International * * * * *

NEWS 1 Web Page URLs for STN Seminar Schedule - N. America
NEWS 2 "Ask CAS" for self-help around the clock
NEWS 3 FEB 27 New STN AnaVist pricing effective March 1, 2006
NEWS 4 MAY 10 CA/CAPLUS enhanced with 1900-1906 U.S. patent records
NEWS 5 MAY 11 KOREAPAT updates resume
NEWS 6 MAY 19 Derwent World Patents Index to be reloaded and enhanced
NEWS 7 MAY 30 IPC 8 Rolled-up Core codes added to CA/CAPLUS and
USPATFULL/USPAT2
NEWS 8 MAY 30 The F-Term thesaurus is now available in CA/CAPLUS
NEWS 9 JUN 02 The first reclassification of IPC codes now complete in
INPADOC
NEWS 10 JUN 26 TULSA/TULSA2 reloaded and enhanced with new search and
and display fields
NEWS 11 JUN 28 Price changes in full-text patent databases EPFULL and PCTFULL
NEWS 12 JUL 11 CHEMSAFE reloaded and enhanced
NEWS 13 JUL 14 FSTA enhanced with Japanese patents
NEWS 14 JUL 19 Coverage of Research Disclosure reinstated in DWPI
NEWS 15 AUG 09 INSPEC enhanced with 1898-1968 archive
NEWS 16 AUG 28 ADISCTI Reloaded and Enhanced
NEWS 17 AUG 30 CA(SM)/CAPLUS(SM) Austrian patent law changes
NEWS 18 SEP 11 CA/CAPLUS enhanced with more pre-1907 records
NEWS 19 SEP 21 CA/CAPLUS fields enhanced with simultaneous left and right
truncation
NEWS 20 SEP 25 CA(SM)/CAPLUS(SM) display of CA Lexicon enhanced
NEWS 21 SEP 25 CAS REGISTRY(SM) no longer includes Concord 3D coordinates
NEWS 22 SEP 25 CAS REGISTRY(SM) updated with amino acid codes for pyrrolysine
NEWS 23 SEP 28 CEABA-VTB classification code fields reloaded with new
classification scheme

NEWS EXPRESS JUNE 30 CURRENT WINDOWS VERSION IS V8.01b, CURRENT
MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
AND CURRENT DISCOVER FILE IS DATED 26 JUNE 2006.

NEWS HOURS STN Operating Hours Plus Help Desk Availability
NEWS LOGIN Welcome Banner and News Items
NEWS IPC8 For general information regarding STN implementation of IPC 8
NEWS X25 X.25 communication option no longer available

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* * * * * STN Columbus * * * * *

FILE 'HOME' ENTERED AT 13:47:15 ON 11 OCT 2006

=>

Uploading

THIS COMMAND NOT AVAILABLE IN THE CURRENT FILE

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Choice (Y/n):

Switching to the Registry File...

Some commands only work in certain files. For example, the EXPAND command can only be used to look at the index in a file which has an index. Enter "HELP COMMANDS" at an arrow prompt (=>) for a list of commands which can be used in this file.

=> FILE REGISTRY

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 13:47:33 ON 11 OCT 2006

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STRUCTURE FILE UPDATES: 10 OCT 2006 HIGHEST RN 910095-75-9

DICTIONARY FILE UPDATES: 10 OCT 2006 HIGHEST RN 910095-75-9

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH June 30, 2006

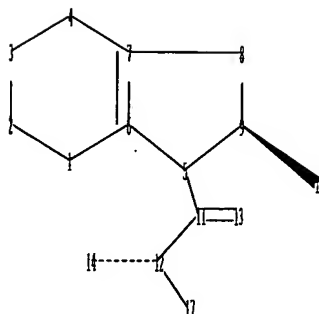
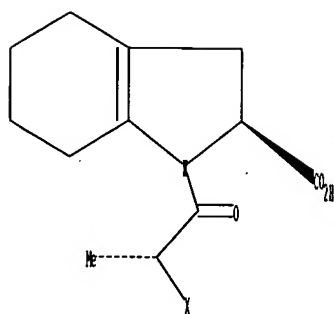
Please note that search-term pricing does apply when conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

<http://www.cas.org/ONLINE/UG/regprops.html>

=>

Uploading C:\Program Files\Stnexp\Queries\10566558.str



chain nodes :

10 11 12 13 14 17

ring nodes :

1 2 3 4 5 6 7 8 9

chain bonds :

5-11 9-10 11-12 11-13 12-14 12-17

ring bonds :

1-2 1-6 2-3 3-4 4-7 5-6 5-9 6-7 7-8 8-9

exact/norm bonds :

5-6 5-9 5-11 11-13 12-14

exact bonds :

1-2 1-6 2-3 3-4 4-7 6-7 7-8 8-9 9-10 11-12 12-17

isolated ring systems :

containing 1 :

G1:X

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:CLASS
11:CLASS 12:CLASS 13:CLASS 14:CLASS 17:CLASS

Stereo Bonds:

10-9 (Single Wedge).

Stereo Chiral Centers:

9 (Parity=Don't Care)

Stereo RSS Sets:

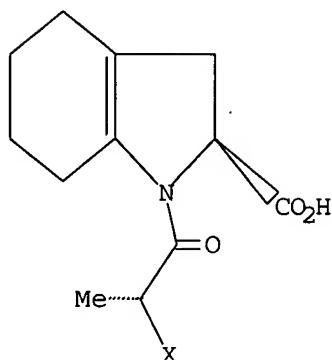
Type=Relative (Default). 1 Nodes= 9

L1 STRUCTURE UPLOADED

=> d l1

L1 HAS NO ANSWERS

L1 STR



G1 X

Structure attributes must be viewed using STN Express query preparation.

=> s l1

SAMPLE SEARCH INITIATED 13:47:47 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 5 TO ITERATE

100.0% PROCESSED 5 ITERATIONS 0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 5 TO 234
PROJECTED ANSWERS: 0 TO 0

L2 0 SEA SSS SAM L1

=> s l1 sss full

FULL SEARCH INITIATED 13:47:53 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 84 TO ITERATE

100.0% PROCESSED 84 ITERATIONS
SEARCH TIME: 00.00.01

1 ANSWERS

L3 1 SEA SSS FUL L1

=> FIL HCAPLUS

COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	166.94	167.15

FILE 'HCAPLUS' ENTERED AT 13:47:59 ON 11 OCT 2006
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FILE COVERS 1907 - 11 Oct 2006 VOL 145 ISS 16
FILE LAST UPDATED: 10 Oct 2006 (20061010/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l3
L4

2 L3

=> d l4 ibib abs hitstr tot

L4 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2006 ACS ON STN
ACCESSION NUMBER: 2005:1311320 HCAPLUS
DOCUMENT NUMBER: 144:7101
TITLE: Method for synthesis of perindopril and its
pharmaceutically acceptable salts
INVENTOR(S): Fugier, Claude; Dubuffet, Thierry; Langlois, Pascal
PATENT ASSIGNEE(S): Adipac Compagnie, Fr.
SOURCE: Eur. Pat. Appl., 9 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1367063	A1	20031203	EP 2003-291931	20030731
EP 1367063	B1	20060823		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
AU 2004261439	A1	20050210	AU 2004-261439	20040729
CA 2533005	AA	20050210	CA 2004-2533005	20040729
WO 2005012333	A2	20050210	WO 2004-FR2035	20040729
WO 2005012333	A3	20050324		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CN 1826352	A	20060830	CN 2004-80021209	20040729
US 2006183920	A1	20060817	US 2006-566562	20060131
NO 2006000922	A	20060224	NO 2006-922	20060224
PRIORITY APPLN. INFO.:			EP 2003-291931	A 20030731
			WO 2004-FR2035	W 20040729

OTHER SOURCE(S): MARPAT 144:7101

AB A method for the synthesis of perindopril [(2S,3aS,7aS)-1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butylamino]propionyl]octahydro-1H-indole-2-carboxylic acid] involves coupling of (2S)-hexahydroindole-2-carboxylic acid or its benzyl ester with (R)-G-CHMeCOCl (G = Cl, Br, OH, tosyloxy, mesyloxy or trifluoromethanesulfonyloxy) and then (S)-Et 2-aminopentanoate, followed by catalytic hydrogenation. In an example, the resp. coupling reactions were carried in CH₂Cl₂-EtNPr-i₂ at room temperature and MeCN-Et₃N at reflux. Yield of perindopril following hydrogenation was 95% (enantiomeric purity 99%).

IT 870152-15-1P

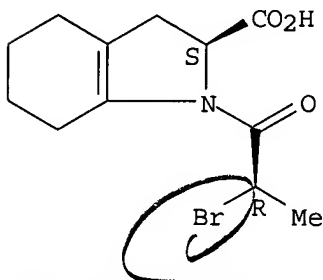
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(synthesis of perindopril from hexahydroindolecarboxylate and bromopropionyl chloride)

RN 870152-15-1 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2R)-2-bromo-1-oxopropyl]-2,3,4,5,6,7-hexahydro-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT:

3

THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:1311047 HCAPLUS

DOCUMENT NUMBER: 144:7100

TITLE: Method for synthesis of perindopril and its pharmaceutically acceptable salts

INVENTOR(S): Fugier, Claude; Dubuffet, Thierry; Langlois, Pascal

PATENT ASSIGNEE(S): Adir et Compagnie, Fr.

SOURCE: Eur. Pat. Appl., 9 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: French

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1367062	A1	20031203	EP 2003-291930	20030731
EP 1367062	B1	20060826		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
AU 2004261440	A1	20050210	AU 2004-261440	20040729
WO 2005012328	A2	20050210	WO 2004-FR2036	20040729
WO 2005012328	A3	20050324		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,				

GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
 LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
 NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
 TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
 RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
 AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
 EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
 SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
 SN, TD, TG

CN 1826351 A 20060830 CN 2004-80021208 20040729
 US 2006189813 A1 20060824 US 2006-566558 20060131
 PRIORITY APPLN. INFO.: EP 2003-291930 A 20030731
 WO 2004-FR2036 W 20040729

OTHER SOURCE(S): CASREACT 144:7100; MARPAT 144:7100

AB A method for the synthesis of perindopril [(2S,3aS,7aS)-1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butylamino]propionyl]octahydro-1H-indole-2-carboxylic acid] involves coupling of (2S)-hexahydroindole-2-carboxylic acid or its benzyl ester with (R)-G-CHMeCOCl (G = Cl, Br, OH, tosyloxy, mesyloxy or trifluoromethanesulfonyloxy) and then (S)-Et 2-aminopentanoate, followed by catalytic hydrogenation. In an example, the resp. coupling reactions were carried in CH₂Cl₂-EtNPr-i₂ at room temperature and MeCN-Et₃N at reflux. Yield of perindopril following hydrogenation was 95% (enantiomeric purity 99%).

IT 870152-15-1P

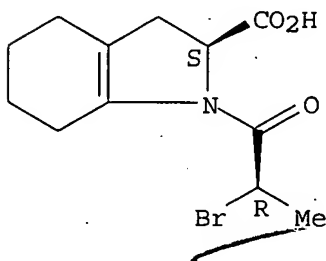
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(synthesis of perindopril from hexahydroindolecarboxylate and bromopropionyl chloride)

RN 870152-15-1 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2R)-2-bromo-1-oxopropyl]-2,3,4,5,6,7-hexahydro-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> FIL REGISTRY

COST IN U.S. DOLLARS

SINCE FILE ENTRY	TOTAL SESSION
17.81	184.96

FULL ESTIMATED COST

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE ENTRY	TOTAL SESSION
-1.50	-1.50

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STRUCTURE FILE UPDATES: 10 OCT 2006 HIGHEST RN 910095-75-9
DICTIONARY FILE UPDATES: 10 OCT 2006 HIGHEST RN 910095-75-9

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TSCA INFORMATION NOW CURRENT THROUGH June 30, 2006

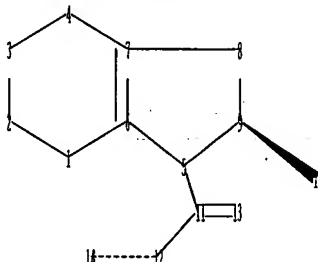
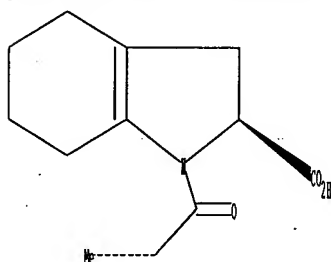
Please note that search-term pricing does apply when
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REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document. For information
on property searching in REGISTRY, refer to:

<http://www.cas.org/ONLINE/UG/regprops.html>

=>

Uploading C:\Program Files\Stnexp\Queries\10566558a.str



chain nodes :
10 11 12 13 14
ring nodes :
1 2 3 4 5 6 7 8 9
chain bonds :
5-11 9-10 11-12 11-13 12-14
ring bonds :
1-2 1-6 2-3 3-4 4-7 5-6 5-9 6-7 7-8 8-9
exact/norm bonds :
5-6 5-9 5-11 11-13 12-14
exact bonds :
1-2 1-6 2-3 3-4 4-7 6-7 7-8 8-9 9-10 11-12
isolated ring systems :
containing 1 :

G1:X

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:CLASS
11:CLASS 12:CLASS 13:CLASS 14:CLASS

Stereo Bonds:

10/11/2006 10566558.trn

10-9 (Single Wedge).

Stereo Chiral Centers:

9 (Parity=Don't Care)

Stereo RSS Sets:

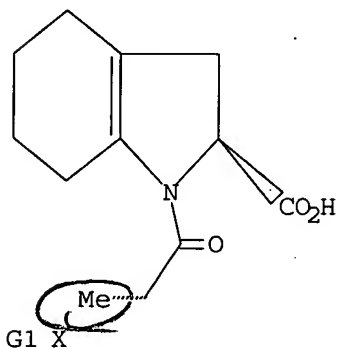
Type=Relative (Default). 1 Nodes= 9

L5 STRUCTURE UPLOADED

=> d 15

L5 HAS NO ANSWERS

L5 STR



Structure attributes must be viewed using STN Express query preparation.

=> s 15

SAMPLE SEARCH INITIATED 13:50:07 FILE 'REGISTRY'

SAMPLE SCREEN SEARCH COMPLETED - 43 TO ITERATE

100.0% PROCESSED 43 ITERATIONS

1 ANSWERS

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**

BATCH **COMPLETE**

PROJECTED ITERATIONS: 467 TO 1253

PROJECTED ANSWERS: 1 TO 80

L6 1 SEA SSS SAM L5

=> s 15 sss full

FULL SEARCH INITIATED 13:50:15 FILE 'REGISTRY'

FULL SCREEN SEARCH COMPLETED - 808 TO ITERATE

100.0% PROCESSED 808 ITERATIONS

SEARCH TIME: 00.00.01

L7 4 SEA SSS FUL L5

=> FIL HCAPLUS

4 ANSWERS

10/11/2006 10566558.trn

COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	167.38	352.34
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
	ENTRY	SESSION
CA SUBSCRIBER PRICE	0.00	-1.50

FILE 'HCAPLUS' ENTERED AT 13:50:42 ON 11 OCT 2006
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FILE COVERS 1907 - 11 Oct 2006 VOL 145 ISS 16
FILE LAST UPDATED: 10 Oct 2006 (20061010/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l7

L8

6 L7

=> d l8 ibib abs hitstr tot

L8 ANSWER 1 OF 6 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:1311320 HCAPLUS

DOCUMENT NUMBER: 144:7101

TITLE: Method for synthesis of perindopril and its pharmaceutically acceptable salts

INVENTOR(S): Fugier, Claude; Dubuffet, Thierry; Langlois, Pascal

PATENT ASSIGNEE(S): Adir et Compagnie, Fr.

SOURCE: Eur. Pat. Appl., 9 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: French

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1367063	A1	20031203	EP 2003-291931	20030731
EP 1367063	B1	20060823		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
AU 2004261439	A1	20050210	AU 2004-261439	20040729
CA 2533005	AA	20050210	CA 2004-2533005	20040729

WO 2005012333 A2 20050210 WO 2004-FR2035 20040729
 WO 2005012333 A3 20050324

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
 CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
 GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
 LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
 NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
 TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
 RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
 AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
 EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
 SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
 SN, TD, TG

CN 1826352 A 20060830 CN 2004-80021209 20040729
 US 2006183920 A1 20060817 US 2006-566562 20060131
 NO 2006000922 A 20060224 NO 2006-922 20060224

PRIORITY APPLN. INFO.:

EP 2003-291931 A 20030731
 WO 2004-FR2035 W 20040729

OTHER SOURCE(S): MARPAT 144:7101

AB A method for the synthesis of perindopril [(2S,3aS,7aS)-1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butylamino]propionyl]octahydro-1H-indole-2-carboxylic acid] involves coupling of (2S)-hexahydroindole-2-carboxylic acid or its benzyl ester with (R)-G-CHMeCOCl (G = Cl, Br, OH, tosyloxy, mesyloxy or trifluoromethanesulfonyloxy) and then (S)-Et 2-aminopentanoate, followed by catalytic hydrogenation. In an example, the resp. coupling reactions were carried in CH₂Cl₂-EtNPr-i₂ at room temperature and MeCN-Et₃N at reflux. Yield of perindopril following hydrogenation was 95% (enantiomeric purity 99%).

IT 625095-50-3P 870152-15-1P

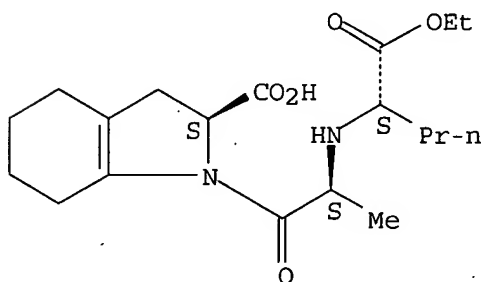
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(synthesis of perindopril from hexahydroindolecarboxylate and bromopropionyl chloride)

RN 625095-50-3 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]-2,3,4,5,6,7-hexahydro-, (2S)-(9CI) (CA INDEX NAME)

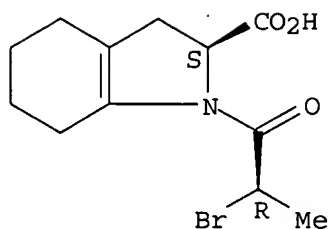
Absolute stereochemistry.



RN 870152-15-1 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2R)-2-bromo-1-oxopropyl]-2,3,4,5,6,7-hexahydro-, (2S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 2 OF 6 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:1311047 HCAPLUS

DOCUMENT NUMBER: 144:7100

TITLE: Method for synthesis of perindopril and its pharmaceutically acceptable salts

INVENTOR(S): Eugier, Claude; Dubuffet, Thierry; Langlois, Pascal

PATENT ASSIGNEE(S): Adir et Compagnie, Fr.

SOURCE: Eur. Pat. Appl., 9 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: French

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1367062	A1	20031203	EP 2003-291930	20030731
EP 1367062	B1	20060830		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
AU 2004261440	A1	20050210	AU 2004-261440	20040729
WO 2005012328	A2	20050210	WO 2004-FR2036	20040729
WO 2005012328	A3	20050324		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CN 1826351	A	20060830	CN 2004-80021208	20040729
US 2006189813	A1	20060824	US 2006-566558	20060131
PRIORITY APPLN. INFO.:			EP 2003-291930	A 20030731
			WO 2004-FR2036	W 20040729

OTHER SOURCE(S): CASREACT 144:7100; MARPAT 144:7100

AB A method for the synthesis of perindopril [(2S,3aS,7aS)-1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butylamino]propionyl]octahydro-1H-indole-2-carboxylic acid] involves coupling of (2S)-hexahydroindole-2-carboxylic acid or its benzyl ester with (R)-G-CHMeCOCl (G = Cl, Br, OH, tosyloxy, mesyloxy or trifluoromethanesulfonyloxy) and then (S)-Et 2-aminopentanoate, followed by catalytic hydrogenation. In an example, the resp. coupling reactions

were carried in CH₂Cl₂-Et₃N at room temperature and MeCN-Et₃N at reflux. Yield of perindopril following hydrogenation was 95% (enantiomeric purity 99%).

IT 625095-50-3P 870152-15-1P

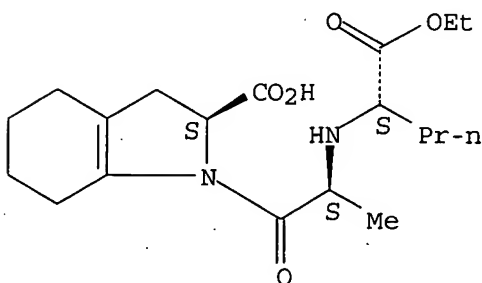
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(synthesis of perindopril from hexahydroindolecarboxylate and bromopropionyl chloride)

RN 625095-50-3 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]-2,3,4,5,6,7-hexahydro-, (2S)-(9CI) (CA INDEX NAME)

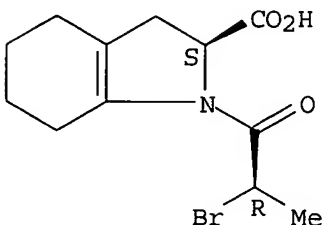
Absolute stereochemistry.



RN 870152-15-1 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2R)-2-bromo-1-oxopropyl]-2,3,4,5,6,7-hexahydro-, (2S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 3 OF 6 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:36708 HCAPLUS

DOCUMENT NUMBER: 140:59938

TITLE: Method for synthesis of perindopril and its pharmaceutically acceptable salts

INVENTOR(S): Dubuffet, Thierry; Lecouve, Jean-Pierre

PATENT ASSIGNEE(S): Les Laboratoires Servier, Fr.

SOURCE: Eur. Pat. Appl., 9 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

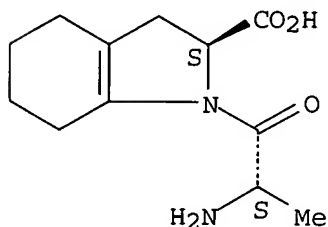
LANGUAGE: French

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1380590	A1	20040114	EP 2003-292131	20030829
EP 1380590	B1	20060906		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
AU 2004270427	A1	20050317	AU 2004-270427	20040827
WO 2005023841	A1	20050317	WO 2004-FR2196	20040827
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CN 1839147	A	20060927	CN 2004-80024192	20040827
PRIORITY APPLN. INFO.:			EP 2003-292131	A 20030829
			WO 2004-FR2196	W 20040827
OTHER SOURCE(S): CASREACT 140:59938; MARPAT 140:59938				
AB A method for the synthesis of perindopril and its pharmaceutically-acceptable salts involves coupling of (2S)-2,3,4,5,6,7-hexahydro-1H-indolecarboxylic acid or its benzyl ester with R ² -L-Ala-X (R ² is a protective group, X is halo), followed by deprotection, reaction with (R)-PrCH(G)CO ₂ Et (G is Cl, Br, I, or tosyloxy), and catalytic hydrogenation. Addition of tert-butylamine to perindopril provides the salt.				
IT 639067-45-1P				
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)				
(preparation of perindopril and tert-butylamine salt)				
RN 639067-45-1 HCAPLUS				
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-amino-1-oxopropyl]-2,3,4,5,6,7-hexahydro-, (2S)- (9CI) (CA INDEX NAME)				

Absolute stereochemistry.



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 4 OF 6 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:947713 HCAPLUS

DOCUMENT NUMBER: 139:381760

TITLE: Method for synthesis of perindopril and its pharmaceutically acceptable salts

INVENTOR(S): Dubuffet, Thierry; Lecouve, Jean-Pierre

PATENT ASSIGNEE(S): Les Laboratoires Servier, Fr.
 SOURCE: Eur. Pat. Appl., 8 pp.
 CODEN: EPXXDW
 DOCUMENT TYPE: Patent
 LANGUAGE: French
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1367061	A1	20031203	EP 2003-291601	20030630
EP 1367061	B1	20060104		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
AT 315043	E	20060215	AT 2003-291601	20030630
ES 2256689	T3	20060716	ES 2003-3291601	20030630
AU 2004253721	A1	20050113	AU 2004-253721	20040628
WO 2005003153	A1	20050113	WO 2004-FR1637	20040628
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CN 1802384	A	20060712	CN 2004-80016014	20040628
US 2006178421	A1	20060810	US 2005-562490	20051222
PRIORITY APPLN. INFO.:			EP 2003-291601	A 20030630
			WO 2004-FR1637	W 20040628

OTHER SOURCE(S): CASREACT 139:381760; MARPAT 139:381760

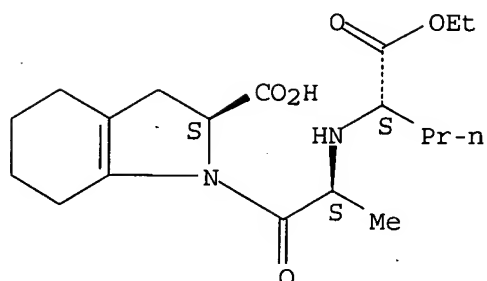
AB A method for the synthesis of perindopril and its pharmaceutically-acceptable salts (e.g., the tert-butylamine) involves cyclocondensation reaction of N-[(S)-1-carbethoxybutyl]-(S)-alanine with sulfinyl chlorides R1SOCl (R1 = imidazolyl, benimidazolyl, or tetrazolyl) to give Et (2S)-2-[(4S)-4-methyl-2,5-dioxo-1,2,3-oxathiazolidin-3-yl]pentanoate, which is amidated with (2S)-2,3,4,5,6,7-hexahydro-1H-indole-2-carboxylic acid and hydrogenated over 10% Pt/C to give perindopril.

IT 625095-50-3P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (synthesis of perindopril via cyclocondensation of carbethoxybutylalanine with imidazolesulfinyl chloride)

RN 625095-50-3 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]-2,3,4,5,6,7-hexahydro-, (2S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 5 OF 6 HCAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 2003:909172 HCAPLUS
 DOCUMENT NUMBER: 139:396166
 TITLE: Method for synthesis of perindopril and its pharmaceutically acceptable salts
 INVENTOR(S): Dubuffet, Thierry; Lecouve, Jean-Pierre
 PATENT ASSIGNEE(S): Les Laboratoires Servier, Fr.
 SOURCE: Eur. Pat. Appl., 8 pp.
 CODEN: EPXXDW
 DOCUMENT TYPE: Patent
 LANGUAGE: French
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1362864	A1	20031119	EP 2003-291600	20030630
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
AU 2004255899	A1	20050120	AU 2004-255899	20040628
WO 2005005461	A2	20050120	WO 2004-FR1638	20040628
WO 2005005461	A3	20050331		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CN 1805972	A	20060719	CN 2004-80016324	20040628
US 2006148884	A1	20060706	US 2005-562950	20051223
PRIORITY APPLN. INFO.:			EP 2003-291600	A 20030630
			WO 2004-FR1638	W 20040628

OTHER SOURCE(S): CASREACT 139:396166; MARPAT 139:396166
 AB Perindopril and its pharmaceutically acceptable salts (e.g., tert-butylamine salt) are prepared by the cyclocondensation reaction of N-[(S)-carboethoxy-1-butyl]-(S)-alanine with a carbonyl compound X1COX2 (X1, X2 = leaving group; e.g., 1,1'-carbonyldiimidazole) to give Et (2S)-2-[(4S)-4-Methyl-2,5-dioxo-1,3-oxazolidin-3-yl]pentanoate which is

amidated with (2S)-2,3,4,5,6,7-hexahydro-1H-indole-2-carboxylic acid in the presence of an acid (e.g., hydrochloric acid) to give (2S)-1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butylamino]propionyl]-2,3,4,5,6,7-hexahydro-1H-indole-2-carboxylic acid which is hydrogenated with a 10% Pt/C catalyst to give perindopril which is then salified with tert-butylamine to give perindopril tert-butylammonium salt.

IT 625095-50-3P

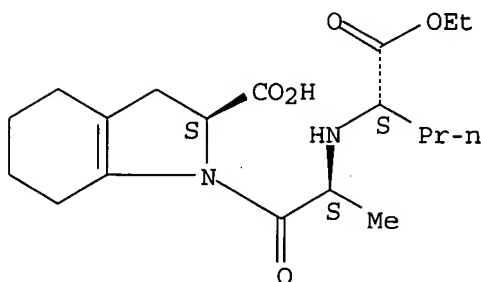
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(intermediate; in a method for synthesis of perindopril and its pharmaceutically acceptable salts)

RN 625095-50-3 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]-2,3,4,5,6,7-hexahydro-, (2S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 6 OF 6 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:470308 HCAPLUS

DOCUMENT NUMBER: 139:22502

TITLE: Method for the synthesis of (2S,3aS,7aS)-1-[(S)-alanyl]octahydro-1H-indole-2-carboxylic acid derivatives for use in the synthesis of perindopril

INVENTOR(S): Dubuffet, Thierry; Lecouve, Jean-Pierre

PATENT ASSIGNEE(S): Les Laboratoires Servier, Fr.

SOURCE: Eur. Pat. Appl., 10 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: French

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1319668	A1	<u>20030618</u>	EP 2003-290606	20030312
EP 1319668	B1	20041027		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
AT 280775	E	20041115	AT 2003-290606	20030312
PT 1319668	T	20050228	PT 2003-290606	20030312
ES 2231759	T3	20050516	ES 2003-3290606	20030312
WO 2004082357	A2	20040930	WO 2004-FR593	20040312
WO 2004082357	A3	20041028		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
 RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:

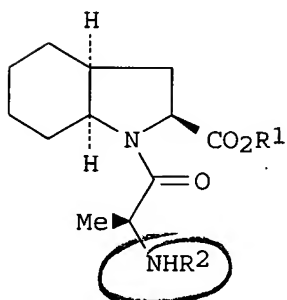
EP 2003-290606

A 20030312

OTHER SOURCE(S):

CASREACT 139:22502; MARPAT 139:22502

GI



AB Alanyloctahydroindolecarboxylic acid derivs. I (R1 is H, alkyl, or benzyl; R2 is a protecting group) were prepared from 2,7-oxepanedione by a multistep procedure, i.e., reaction with (R)-XCH₂CH(NHR₃)CO₂R₄ (X is Br or iodo; R₃ is a protecting group; R₄ is benzyl or alkyl), cyclization of deprotected 2-amino-4-oxononanedioic acid derivative, Ti-catalyzed coupling to form the indole ring system, reaction with an alanine derivs., and catalytic hydrogenation. In an example, I (R1 = H, R2 = tert-butoxycarbonyl) was obtained with enantiomeric purity 99%.

IT 537014-87-2P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(synthesis of alanyloctahydroindolecarboxylic acid derivs. for use in synthesis of perindopril)

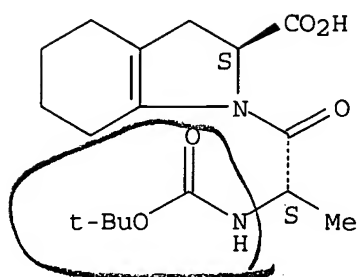
RN 537014-87-2 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1,1-dimethylethoxy)carbonyl]amino]-1-oxopropyl]-2,3,4,5,6,7-hexahydro-, (2S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

10/11/2006

10566558.trn



REFERENCE COUNT:

3

THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

33.19

385.53

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE

TOTAL

ENTRY

SESSION

CA SUBSCRIBER PRICE

-4.50

-6.00

STN INTERNATIONAL LOGOFF AT 13:51:19 ON 11 OCT 2006